

REMARKS

By this response, Applicants cancel claims 50-52 without prejudice and without disclaimer of the subject matter contained therein. Applicants respectfully reserve their right to pursue the subject matter of the canceled claims in one or more continuing application(s). Claims 1-14, 29-31, 33-39, and 46-53 are pending in this application.

Applicants note with appreciation the indication that the period for response to the September 24, 2003 Office Action was, in fact, reset on October 25, 2004.

Applicants appreciate the clarification as to which claims are pending in the application and their treatment: Claims 1-14, 29-31, 33-39, 45-47, and 53 were examined as the Group I election, and claims 48-52 have apparently been examined and will be rejoined upon determination of allowable subject matter in those claims.

Again, Applicants note with appreciation the indication at page 2 that claims 1-14, 29-31, 33-39, 45-47 and 53 are allowed. We note, however, that the Office Action Summary differs from the body of the action, indicating only that claims 1-14, 29-31, and 33-39 are allowed. Applicants believe this is an inadvertent error, since no rejection is directed to claims 45-47 within the body of the Office Action. Thus, in the absence of any rejection, it appears that the indication on page 2 that claims 45-47 are allowable is correct. Confirmation of the same is respectfully requested.

35 U.S.C. § 112

Claims 48-52 stand rejected for allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The action provides guidance as to how this possession might be

established, on page 4, where the action indications the "specification does not adequately describe the nexus between TACE and matrix metalloproteinases and a useful treatment of a disease/condition."

Claims 48 and 49 are directed to methods of inhibiting pathological changes mediated by TNF-alpha converting enzymes (TACE). Claim 49 recites several specific disorders to be treated. The art is replete with examples providing the nexus between TACE and many diseases/conditions. TNF- α is a pro-inflammatory cytokine that is believed to have a role in **rheumatoid arthritis** [Shire, M. G.; Muller, G. W. *Exp. Opin. Ther. Patents* 1998, 8(5), 531; Grossman, J. M.; Brahn, E. J. *Women's Health* 1997, 6(6), 627; Isomaki, P.; Punnonen, J. *Ann. Med.* 1997, 29, 499; Camussi, G.; Lupia, E. *Drugs*, 1998, 55(5), 613], **septic shock** [Mathison, et. al. *J. Clin. Invest.* 1988, 81, 1925; Miethke, et. al. *J. Exp. Med.* 1992, 175, 91], **graft rejection** [Piguet, P. F.; Grau, G. E.; et al. *J. Exp. Med.* 1987, 166, 1280], **cachexia** [Beutler, B.; Cerami, A. *Ann. Rev. Biochem.* 1988, 57, 505], anorexia, **inflammation** [Ksontini, R.; MacKay, S. L. D.; Moldawer, L. L. *Arch. Surg.* 1998, 133, 558], **congestive heart failure** [Packer, M. *Circulation*, 1995, 92(6), 1379; Ferrari, R.; Bachetti, T.; et. al. *Circulation*, 1995, 92(6), 1479], post-ischaemic reperfusion injury, **inflammatory disease of the central nervous system**, **inflammatory bowel disease**, **insulin resistance** [Hotamisligil, G. S.; Shargill, N. S.; Spiegelman, B. M.; et. al. *Science*, 1993, 259, 87] and **HIV infection** [Peterson, P. K.; Gekker, G.; et. al. *J. Clin. Invest.* 1992, 89, 574; Pallares-Trujillo, J.; Lopez-Soriano, F. J. Argiles, J. M. *Med. Res. Reviews*, 1995, 15 (6), 533], in addition to its well-documented antitumor properties [Old, L. *Science*, 1985, 230, 630].

The nexus between TACE and each of the specific disorders/conditions claimed in claim 49 are encompassed by the references listed above (and emphasized in bold), with the exception of fever, which it will readily be recognized often accompanies many of the other conditions and therefore can be similarly treated. The references also provide the nexus

between TACE and several other diseases/conditions. Thus, those of skill in the art are aware of diseases or conditions brought about by pathological changes mediated by TACE, and therefore would readily recognize the nexus between TACE and such diseases and conditions.

Accordingly, Applicants respectfully assert that they have described the subject matter of claims 48 and 49 sufficiently to reasonably convey they were in possession at the time of filing. Withdrawal of the rejection under 35 U.S.C. § 112 is respectfully requested.

Claims 50-52 were directed to methods of inhibiting pathological changes mediated by matrix metalloproteinases and have been canceled, thereby rendering the rejection thereof moot.

Applicants respectfully submit that all pending claims are in condition for allowance.

The Commissioner is hereby authorized to charge any fee or underpayment thereof or credit any overpayment to deposit account no. 50-1275.

Early reconsideration and allowance of all pending claims is respectfully requested. The examiner is requested to contact the undersigned attorney if an interview, telephonic or personal, would facilitate allowance of the claims.

Respectfully submitted,
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